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13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

The focus of this study is adaptive radiation therapy (ART) for prostate cancer, in which the treatment is to be adjusted over time, based on CT images acquired on the treatment table before each daily treatment. The goals are twofold: We seek to make ART for prostate cancer *possible*, and we seek to evaluate how *useful* it will be. As steps toward making it possible, we have developed software tools to localize the areas to be targeted or avoided, and to evaluate the motion of the tissue from day to day. We have produced a tool called ImMap that can perform these tasks, and are beginning to study its reliability and effectiveness. To evaluate the utility of ART, we are using a data set consisting of repeated CT scans from approximately 20 treatment days for five anonymous cancer subjects, along with manual segmentations of the prostate, bladder, and rectum for each subject and each day. We have evaluated the motion of the body due to setup error, and are preparing to evaluate the motions of the organs with respect to the body.

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Introduction

This research involves the potential of treating prostate cancer using adaptive radiotherapy (ART), in which daily treatments are adjusted based on information, typically from previous treatments, about the locations of the tumor and critical healthy tissues. An approach that has been used, and that we are adopting, is to develop a new patient treatment volume (PTV), partway through treatment, that reflects actual motion observed for that patient [Yan 2000; Mageras 1996]. Manual analysis of this information is time consuming, making ART challenging without automated methods. The goal of this work is to develop such methods and evaluate their effectiveness.

Body

We have developed an interactive software package, ImMap, that enables the user to nonrigidly deform an image taken during a daily treatment session (a daily image) to a planning image (task 1a). Using this deformation, organ segmentations outlined on the planning image can be warped to the space of the daily image. We are evaluating these techniques based on patient data with which we have been provided. We have also developed a "batch" program, BeamLock, that can perform the nonrigid image registration, and the corresponding deformations of the organ segmentations, for all the daily images for a given patient.

One component of task 1a is to handle the problem of rectal filling. Rectal gas in particular poses a problem for image registration since no correct correspondence exists between an image that contains gas and one that does not. Standard large-deformation image registration algorithms typically produce bad results in these situations, as they attempt to match a pocket of gas in one image to an image that does not contain gas. To overcome this problem, we have developed a new method to eliminate rectal gas from images before applying image registration. This method automatically determines the location and extent of the gas and then applies a force on the boundary of the gas that deflates the region like a balloon—removing it from the image. After gas deflation, the images are registered and image-to-image correspondence is given by concatenating the gas deflation and image registration transformations. See Appendix.

In large-deformation image registration, there is often a simplifying assumption made that all tissue has the same elastic and mechanical properties. While this is not anatomically correct, accurate registrations can often be estimated anyway. In the pelvic region, however, filling of the bladder and rectum often cause large-deformation motion very close the pelvic bone, which causes the bone to deform and stretch unrealistically. To account for this we are developing within our large-deformation registration framework the ability to spatially vary tissue properties. We have completed an initial implementation where bony anatomy remains rigid during the registration process.

We are engaged in preliminary evaluation of our methods using a data set consisting of repeated CT scans from approximately 20 treatment days for five anonymous cancer subjects, along with manual segmentations of the prostate, bladder, and rectum for each subject and each day.

We have, for one subject, used the organ deformation estimates to compute the actual delivered dose, accumulated over the course of treatment (task 2). We are refining this method to make it more efficient, so that it can be carried out easily for all subjects in the data set. In the subject considered, we found considerably worse dose conformance in the actual cumulative dose than in a hypothetical cumulative dose in which the subject was in exactly the same position

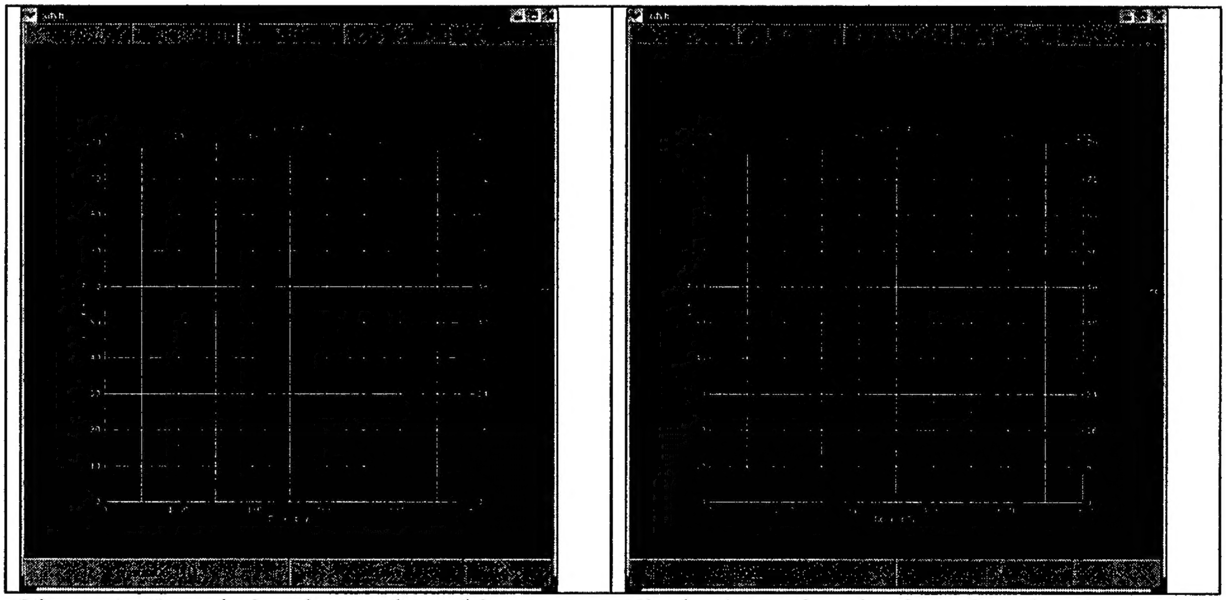

Figure 1: Cumulative dose volume histograms. The horizontal scale gives dose levels up to 7800 Gy, and the vertical scale shows the percent of the PTV receiving the specified dose. The left image is the actual dose given. The right is the hypothetical dose, assuming that no tissue had moved between treatment days.

on each treatment day as on the planning day, with no internal organ motion. This case was simulated using our image-warping software. See Figure 1.

For all five subjects in the data set, we have used ImMap to rigidly align the daily images with the planning image, as a measure of the setup accuracy. The resulting translation vector measures the direction and distance from where in the subject the treatment beams were planned to be, and where they actually were at each treatment. The results are shown in Figure 1 below. Over all the subjects, the standard deviations of the components of the setup error are 4.1 mm in the left-right direction, 2.8 mm in the anterior-posterior direction, and 2.0 mm in the superior-inferior direction. These results can be compared to those, mentioned in the proposal, found at Memorial Sloan Kettering Cancer Center, with standard deviations of 2.7, 2.3, and 2.2 mm respectively [Hanley 1997]. Note that in our results there is also a systematic bias in the vertical (anterior-to-posterior) direction that occurs for four of the subjects. This bias is an issue we are working to resolve.

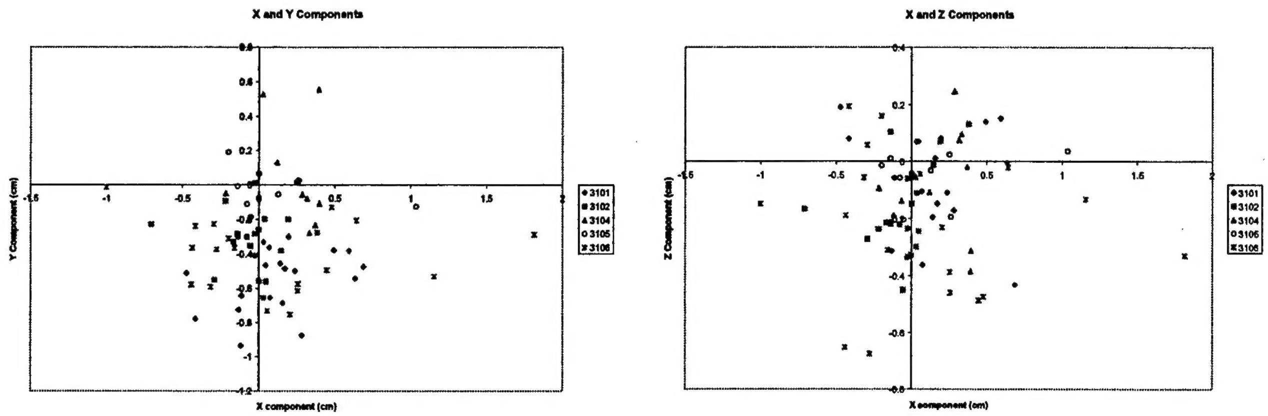

Figure 2: Translation required to align each daily image with the patient planning image, for each of five patients. The x component (from patient's left to right) is the horizontal axis in both images.

Key Research Accomplishments

- ImMap, an interactive package for automated image registration and computer-assisted image segmentation, with visualization.
- BeamLock, a program by which all images for a given subject can be registered to the planning image, and anatomical structures from the planning image thereby deformed to fit the daily images.
- Careful analysis of the nature of the setup error for each subject in a data set.
- Computation of the actual cumulative dose delivered to both the cancerous and critical healthy tissues of one subject.

Reportable Outcomes

Abstracts:

B. Davis, D. Prigent, J. Bechtel, J. Rosenman, D. M. Lovelock, and S. Joshi. Accommodating bowel gas in large deformation image registration for adaptive radiation therapy of the prostate. AAPM 46th Annual Meeting, 2004.

S. Joshi, T. Cullip, B. Davis, S. Chang, P. Keall, Y. Erdi, S. Nehmeh, G. Mageras, and J Rosenman. 4d IMRT optimization accommodating respiratory motion using image mapping. AAPM 46th Annual Meeting, 2004.

P. Wang, D. Lovelock, S. Joshi, B. Davis, G. Mageras, and C. Ling. Evaluation of an automated deformable registration algorithm for localizing the prostate in serial ct image sets. AAPM 46th Annual Meeting, 2004.

A. Pevsner, G. Mageras, S. Joshi, B. Davis, A. Hertanto, E. Yorke, K. Rosenzweig, Y. Erdi, S. Nehmeh, J. Humm, S. Larson, and C. Ling. Evaluation of a deformable matching algorithm for automatic segmentation of lung tumors from respiratory correlated CT data. AAPM 46th Annual Meeting, 2004.

G. Mageras, S. Joshi, B. Davis, A. Pevsner, A. Hertanto, E. Yorke, K. Rosenzweig, and C. Ling. Evaluation of an automated deformable matching method for quantifying lung tumor motion in respiration-correlated CT images. ICCR (Accepted), 2004.

Full Length Conference Papers:

B. Davis, P. Lorenzen, and S. Joshi. Large deformation minimum mean squared error template estimation for computational anatomy. ISBI, 2004.

Conclusions

Of the research completed so far, one of the most significant conclusions is that, even when considerable care is taken, the magnitude of patient setup error is at least comparable to that which we expect due to organ motion. We have also observed that, as expected, the cumulative dose volume histogram differs from the histogram simulated during planning, with more of the treatment volume receiving a subclinical dose in the actual cumulative DVH. It is this last observation that points most directly to the potential utility of adaptive radiation therapy.

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[Yan 2000] D. Yan, D. Lockman, D. Brabbins, L. Tyburski, A. Martinez. An off-line strategy for constructing a patient-specific planning target volume in adaptive treatment process for prostate cancer. Int J Radiat Oncol Biol Phys 48: 289-302, 2000.

Appendix:
Abstract and Supporting Document

B. Davis, D. Prigent, J. Bechtel, J. Rosenman, D. M. Lovelock, and S. Joshi.
Accommodating bowel gas in large deformation image registration for adaptive radiation therapy of the prostate.
AAPM 46th Annual Meeting, 2004.

We have been developing methods for adaptive radiation therapy of the prostate that use large-deformation image registration to automatically track organ motion between inter-treatment CT images. The presence of bowel gas in pelvic CT data can cause significant errors in image registration because no correct correspondence exists between an image that contains gas and one that does not. In order to accommodate bowel gas and improve the accuracy of image registration for adaptive radiation therapy, we propose a novel method for deriving image-to-image correspondence that includes steps for segmenting and deflating bowel gas prior to image registration. First, simple thresholding is used to create a binary image of gas present in the rectum. A non-diffeomorphic deflation transformation is then estimated by generating a flow driven by the gradient of this binary image. The gradient is only non-zero at the boundary of the binary regions, so the gas is effectively deflated like a balloon. Finally, the deflated images are accurately registered using previously developed image registration algorithms. Current research shows that for images without gas, these algorithms are accurate to within 1.5mm. Correspondence between the original images is estimated by concatenating the resulting registration transformation with the appropriate gas deflation transformations. Once this method is used to establish correspondence, delineated anatomical structures are mapped between images, allowing for the analysis of organ morphology. These correspondences are also used to accumulate inter-fraction dose in a common coordinate system. We present results of applying this method to inter-treatment pelvic CT data.

Accommodating Bowel Gas in Large Deformation Image Registration for Adaptive Radiation Therapy of the Prostate

Introduction: One of the major challenges in adaptive radiation therapy is the estimation of accurate correspondence between inter-treatment images. This correspondence can be used to study organ motion and to accumulate inter-fraction dose. We have been using large deformation image registration to estimate correspondence between images. In prostate images, however, the presence of bowel gas can cause significant correspondence errors as the registration algorithm attempts to expand or contract image regions to match pockets of bowel gas. To account for this problem, we present a novel method that combines large deformation image registration with a bowel gas segmentation and deflation algorithm.

Methods: As the contrast between gas and surrounding tissue is very high in CT images, we create a binary segmentation of the gas in an image using a simple thresholding operation . We refine this binary segmentation using a morphological open operation. Next, we construct a deflation transformation s based on a flow induced by the gradient of the binary image. Points along the gas-tissue border, where the gradient is non-zero, flow in the direction of the gradient. As a result, gas filled regions collapse toward their medial skeletons—deflating like a balloon.

More precisely, we consider an image $I(x)$ with associated coordinate system Ω, $x = (x_1, x_2, x_3) \in \Omega \subset \Re^3$. We construct a non-diffeomorphic deflation transformation $s : \Omega \to \Omega$ such that $I(s(x))$ is the image $I(x)$ after a deformation that deflates gas. s is constructed by integrating velocity fields $v(x,t)$ forward in time, i.e. $s(x) = \int_0^1 v(s(x,t),t)\,dt$. These velocity fields are induced by a force function $F(x,t) = \nabla(I \circ s_t)(x)$ that is the gradient of the binary image. The force function and velocity fields are related by the modified Navier-Stokes operator $(\alpha\nabla^2 + \beta\nabla\nabla\cdot + \gamma)v(x,t) = F(x,t)$. We solve for s using an iterative greedy method.

After deflating bowel gas, images can be accurately registered. We apply the theory of large deformation diffeomorphisms [1] to generate a deformation $h : \Omega_1 \to \Omega_2$ that defines a voxel to voxel correspondence between the two images I_1 and $I_2 \circ s$ [2]. Correspondence between the original images I_1 and I_2 is estimated by concatenating the registration and deflation transformations, i.e. $s \circ h : \Omega_1 \to \Omega_2$. This composite transformation is not guaranteed to be diffeomorphic. However, the non-diffeomorphic part of the transformation is restricted to the region of the rectum that contains gas—where no correspondence exists.

Results: All experiments were carried out on 3D intra-patient pelvic CT data. Figure 1 shows an axial slice from rigidly aligned reference and daily images. In this case, correspondence between the reference and daily images is estimated using only large deformation image registration. This correspondence is used to map manually drawn contours of the prostate and rectum from the reference image onto the daily image. Manual contours are drawn in red while mapped contours are drawn in yellow. Notice the misalignment of the manual and automatically generated contours in the daily image; the presence of bowel gas has caused correspondence errors around the rectum. Figure 2 shows the result of our gas deflation algorithm. The large pocket of gas present in the daily image has been deflated, resulting in an image that can be accurately registered to the reference image. Figure 3 shows the result of the method presented in this paper. A more accurate correspondence between the reference and daily images is established by concatenating registration and deflation transformations. Notice the close alignment between the manual contours and the contours generated by our method. We plan a statistical analysis of these results, including measurement of contour overlap statistics, inter-patient variability, and inter-rater variability.

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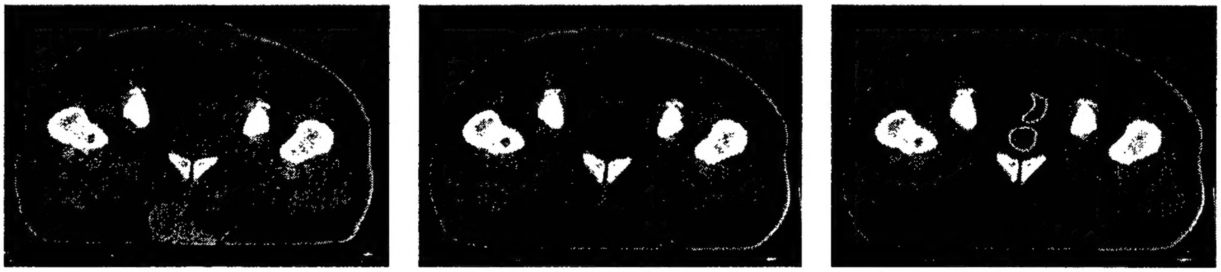
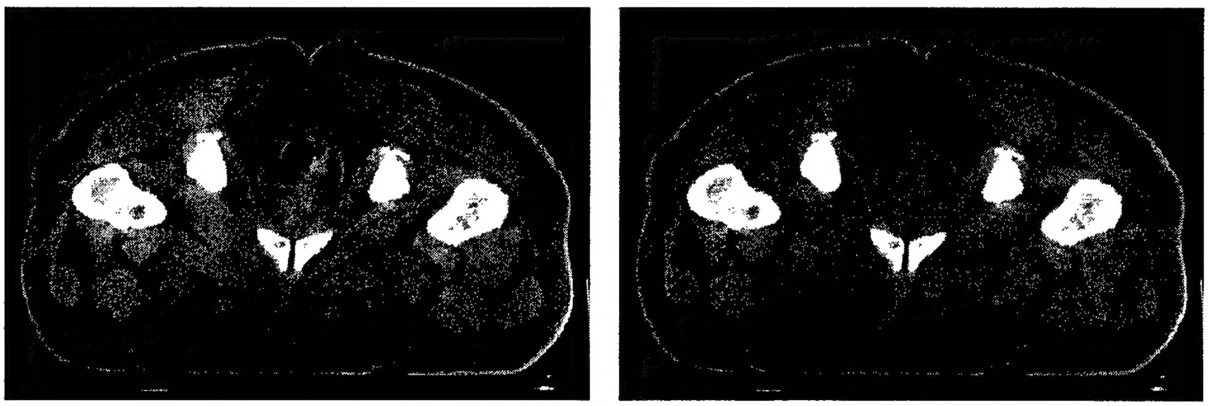
[1] Michael I. Miller, Sarang C. Joshi, and Gary E. Christensen, "Large deformation fluid diffeomorphisms for landmark and image matching," in *Brain Warping*, Arthur W. Toga, Ed., chapter 7. Academic Press, 1999.

[2] Brad Davis, Peter Lorenzen, and Sarang Joshi, "Large deformation minimum mean squared error template estimation for computational anatomy," in *ISBI*, 2004.



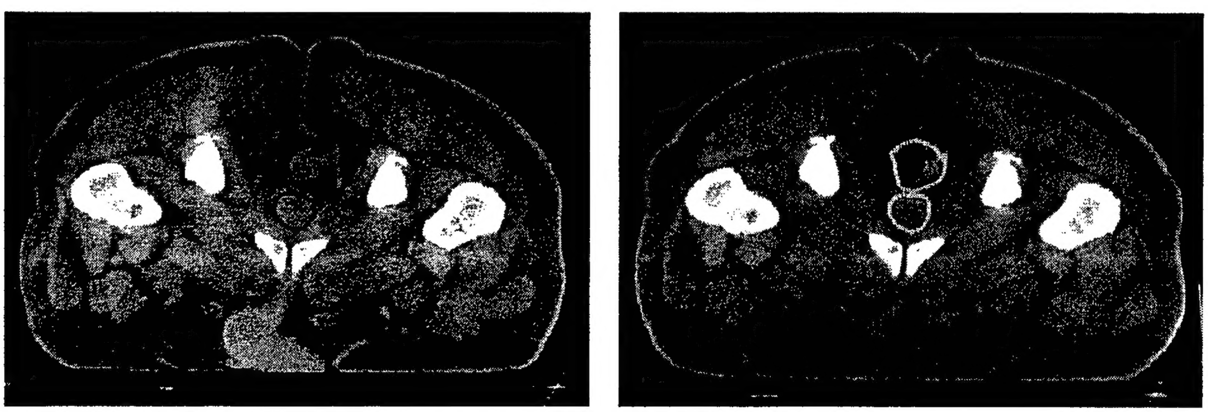
Reference Image | Registered Daily Image | Daily Image

Figure 1: Correspondence is estimated between the reference and daily image without accounting for bowel gas. This correspondence is used to map manually drawn contours of the prostate and rectum from the reference image onto the daily image. Manually drawn contours are shown in red and mapped contours are shown in yellow. Notice the misalignment of the manual and mapped contours near the bowel gas in the daily image.



Daily Image | Deflated Daily Image

Figure 2: Demonstration of our gas deflation algorithm: the gas in the daily image is deflated. The deflated image can be accurately registered to the reference image.



Reference Image | Daily Image

Figure 3: Demonstration of our method for accounting for gas while estimating correspondence. The reference image has been registered to the deflated daily image shown in Figure 2. Correspondence between the reference and daily image is established by concatenating the registration and deflation transformations. Notice the close agreement between the manual (red) and automatically generated (yellow) contours in the daily image.